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## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

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GRESSEL, JONATHAN

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Serial No.: 09/889,737

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Filed: 20 June, 2001

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Science Society (past President and Vice President), International Association for Plant Tissue Culture (past Israel Chapter Chairperson), Weed Science Society of Israel (pats Chairman), Weed Science Society of America (honorary member) and American Society of Plant Biologists, among others (see attached CV). I serve or have served on the editorial board of J. of Agromedicine, Oxford Survey of Plant Molecular and Cell Biology, and Physiologia Plantarum, Pesticide Biochemistry and Physiology, and Plant Science..

I am the inventor of the subject matter claimed in the above-referenced U.S. patent application.

I have read the Official actions issued with respect to the above-identified application.

In this Official action, the Examiner has rejected claims 5-11 under 35 U.S.C. § 112, first paragraph as containing subject matter which was not described in the specification in such a way as to convey to one skilled in the art that the inventors, at the time that the application was filed, had possession of the claimed invention. The Examiner states that the claims are broadly drawn to constructs comprising a multitude of sequences and from a multitude of sources, conferring traits deleterious to weeds such as abolished secondary dormancy, uniform or delayed ripening, anti-shattering, dwarfism, etc., and methods of using such constructs to transform plants, while the specification provides no guidance regarding the isolation of any gene or gene product conferring such traits. The Examiner has further rejected claims 5-11 as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention.

The present pioneering invention is of a method of obtaining a crop capable of mitigating the effects of intra- or interspecies introgression of genetically engineered trait(s) between the transgenic crops and potential

interbreeding weeds or wild species, and of genetic constructs, for preventing transfer of advantageous traits such as herbicide resistance, environmental stress resistance, high productivity, etc. to undesirable varieties of the crop or to related weeds or to related wild species. This novel method represents a revolutionary departure from previously conceived efforts to contain such undesirable transfer of genetically engineered traits into potential interbreeding species, in that fundamental differences between crop cultivation and weed growth are identified, and exploited, to the disadvantage of the undesirable interbreeding species. Previous efforts have depended upon inefficient traditional containment means such as isolation distances (isolation zones) and barrier crops, less conventional, but still problematic biological containment means such as apomixis, cleistogamy, male sterility and plastid transformation and the highly complex and unproven introduction of lethal traits under control of inducible promoters. Further, when any of these previous containment systems are used, they can, at best, merely prevent most gene transfer, but are still inherently "leaky". Thus they may delay introgression of desirable traits to undesirable, related "weedy" species, but cannot completely prevent it. Thus, if the novel trait provides a selective advantage, once containment has been breached and introgression has successfully occurred the trait will quickly disperse throughout the undesirable (weed) population. In stark contrast, the method and constructs of the present invention can suppress and mitigate this dispersal of transgenes within undesirable populations following such a breach of containment. To the best of my knowledge all previous work has been directed towards containment of transgenes, and I am the world's foremost pioneer in conceiving transgenic technologies to mitigate the danger of introgression following breach of containment barriers.

The Examiner has stated that one of ordinary skill in the art would not

be able to make and/or use the present invention as claimed without resorting to undue experimentation. Contrary to the Examiner's contention, the instant specification includes detailed description of methods of identifying a first, desirable genetic trait (see, for example, page 8, lines 8-18), and a second, benign or desirable genetic trait being disadvantageous to an undesirable, uncultivated interbreeding variety of a cultivated crop (see, for example, page 16, line 11 to page 24, line 31), methods of producing tandemly linked constructs therewith, and production of transgenic plants for mitigating the effects of introgression to undesirable "weedy" varieties (page 11, line 19 to page 14, line 27).

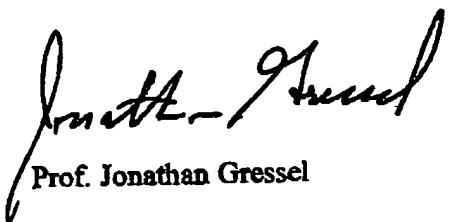
Indeed, employing the methods described in the instant specification, such a tandem construct has recently been produced and transformed into a tobacco plant, resulting in a transgenic tobacco plant having a *ahas*<sup>R</sup> herbicide resistance gene tandemly linked with a *gai* dwarfism gene. Stable, genomic expression of the *ahas*<sup>R</sup> gene conferred resistance to imidizolinone herbicides, but the reduced stature conferred by the semi-dwarfism *gai* gene resulted in decreased survival when co-cultivated among wild-type segregants (see attached Appendix), even though expression of the transgenes actually increased productivity when the transgenic plants were grown alone with only self competition. The reduced competitive ability with wild type tobacco plants was expressed as very low survival rates of the transgenic plants, among the few surviving transgenic individuals when in competition with the non-transgenic wild type. The significance of these results lies in the fact that any offspring that would survive would again be unfit to compete with their normal sibs, meaning that introgressed genes would always remain at a low frequency in the population. This simulates the fate of crop-weed hybrids resulting from unintended introgression of a construct of the present invention to an undesirable, uncultivated interbreeding species of a cultivated crop (tobacco, in this case), when

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competing with wild-type weeds, or such crops as volunteer weeds, when the selector herbicide is not present. Such a demonstration of impaired survival and fitness in the transgenic plants having the tandemly linked herbicide resistance and introgression-mitigating genes, produced according to the teachings of the present invention, confirms both the soundness of the method and the fullness of the enablement therein.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

15 May 2003

A handwritten signature in black ink, appearing to read "Jonathan Gressel".

Prof. Jonathan Gressel

Enc.:

Curriculum Vitae of Prof. Jonathan Gressel

**JONATHAN GRESSEL -CURRICULUM VITAE**

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phone:+972-8-934-3481; fax:+972-8-934-4181 email: [Jonathan.Gressel@weizmann.ac.il](mailto:Jonathan.Gressel@weizmann.ac.il)

**EDUCATION**

1955-1957 Ohio State University - B. Sc. in Plant Sciences  
1957-1959 University of Wisconsin - M. Sc. in Botany (Plant Physiology).  
1959-1962 University of Wisconsin - Ph. D. Botany/Horticulture, Minor: Biochemistry.

**EMPLOYMENT AND STUDY LEAVES (recent)**

1985-present Full Professor - Dept. of Plant Sciences, Weizmann Institute of Science  
1988 Sabbatical (3 months) Biotechnology Affiliates  
1997 Sabbatical (3 months) Iowa State University  
2001 Sabbatical (3 months) Iowa State University

**SCIENCE RELATED ACTIVITIES**

1978-present Member - editorial board, Plant Science Letters now Plant Science  
1982-1984 Chairman, Israel Chapter of the International Association for Plant Tissue Culture.  
1983-1993 Member - editorial board - Oxford Survey of Plant Molecular and Cell Biology.  
1984-1985 Founding chairman - Israel Society for Plant Tissue Culture and Molecular Biology.  
1987-present Member-editorial board, Pesticide Biochemistry and Physiology.  
1990-1992 Chairman, Weed Science Society of Israel  
1992-2000 Editorial Board, Journal of Agromedicine.  
1992-present Advisory Editorial Board - Physiologia Plantarum  
1993-1994 First Israeli Gov't Commission on Release of Transgenic Organisms  
1994-1997 Israel Coordinator, Egypt-Israel-U.S.A. Broomrape Research Program  
1995 Co-chair, Gordon Conference on Agriculture Science.  
1995-1997 Vice-President - International Weed Science Society  
1996-present Area Editor - Resistant Pest Management Newsletter  
1997-1999 President - International Weed Science Society  
1997-2000 Coordinator - COST 815 Broomrape Working Group  
1997-2000 Chairman - Scientific Program Committee - 3<sup>rd</sup> Intl. Weed Science Congress  
2001 - Co-chairman- NATO Workshop "Enhancing Biocontrol Agents and Handling Risks"  
2002 - Lecturer - Univ. Concepcion - UNIDO postgraduate course in transgenic biosafety  
2003 - Co-convenor Africa Regional Consultative Meeting (Part of UNIDO Global Biotechnology Forum)

**SELECTED AWARDS AND RECENT RESEARCH GRANTS**

1979 Cohen Award in Plant Protection of the Israel Agricultural Research  
1989-1990 National Council for Research and Development - Synergizing  
**Mycoherbicides**  
1992- Honorary Fellow - Weed Science Society of America  
1990-1993 Minerva, Control of chloroplast enzymes conferring tolerance to  
photooxidation.  
1992-1996 AID -CDR, Reducing herbicide input to prevent and overcome resistance.  
1992-1995 BARD, Mechanisms of oxidant resistance in weed and crop species  
1993-1997 AID U.S.A.-Egypt-Israel. Use of synergized organisms to control *Orobanche*  
1994-1997 GIARA, Oxygen radicals and lipid peroxidation in drought resistance of  
wheat  
1995-1998 INDO-ISRAEL AGRICULTURAL BIOTECHNOLOGY PROGRAM,  
1995-1998 Israel Ministry of Science - Wheat Transformation Technologies,  
1996-2002 ROCKEFELLER FOUNDATION-Seed treatments for the control of *Striga* in  
maize 1998-2001 SGB – Generating herbicide resistant wheat  
1998-2003 DFG – Biocontrol of broomrape  
1999-2002 EU-INCO –Evaluating risks of transgene introgression  
2000-2001 LEVIN FOUNDATION - Tandem constructs for mitigating gene introgression  
2002-2003 LEVIN FOUNDATION – Developing algorithms for Biobarcoding™

**DEGREES SUPERVISED**

Graduated 7 M.Sc. and 14 Ph.D students

**PUBLICATIONS**

Over 240 peer-reviewed journal articles and invited book chapters; four books: 10 patents

**AREAS OF EXPERTISE**

Plant and fungal physiology, biochemistry and molecular biology

**Specifically:**

Transgenic herbicide resistant crops – needs, generation, uses  
Herbicide resistance – evolution, prevention, genetic and biochemical  
mechanisms  
Herbicide action – mechanisms, synergies, formulations  
Introgression of crop transgenes to weeds – biosafety and mitigating failsafe  
mechanisms  
Parasitic weeds – novel chemical and biological control mechanisms  
Biological control of weeds – chemical synergies, transgenic improvement  
and failsafes